UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MICHAEL MITTMANN,
MACDONALD MORRIS, TOM B. RYDER
and DAVID LOCKHART

Appeal No. 2006-0842
Application No. 09/827,383

HEARD: May 11, 2006

Before SCHEINER, GRIMES and GREEN, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a set of nucleic acids, which the examiner has rejected for lack of patentable utility. We have jurisdiction under 35 U.S.C. § 134. We conclude that the claims are supported by at least one specific and substantial utility, and therefore reverse the rejections on appeal.

Background

"The use of short nucleic acid sequences as 'tags' to identify specific biological substances in a sample is known." Specification, page 2. The specification discloses nucleic acids that are said to provide "sets of tag sequences which are known to

hybridize effectively to their complementary probe sequences with minimal cross-hybridization between the different tag sequences." Id.

An initial set of 2200 sequences was selected to have closely matched melting temperatures and "optimized and standardize[d] . . . hybridization characteristics." Page 8. "The hybridization performance of the entire set of 2200 candidate sequences was evaluated," and the 2050 sequences with "the highest discrimination and signal intensity" were selected. Pages 8 and 9. The 2050 nucleic acids, each twenty nucleotides in length, are shown in the specification's Table 1 (pages 10-53).

The sequences are described as tags that may be used as labels for a wide variety of materials or in screening chemical libraries. Page 9. The specification cites several references and U.S. Patents that are said to disclose such methods:

> For example, tags may be used as a method of or as labels for a wide variety of biological and nonbiological materials, see, for example, Dollinger, The Polymerase Chain Reaction pp. 265-274 . . . or as a method of screening complex chemical libraries. See, for example, Brenner and Lerner, PNAS 89, 5281-5283 (1992); Alper, Science, 264:1399-1401 (1994); and Needels et al. PNAS 90, 10700-10704 (1993). See also US Patent Nos. 4,359,353, 4,441,943, 5,451,505, 5,149,625, 5,654,413 and 5,800,992.

Pages 9-10. The specification also cites patent application 08/626,285 as describing "tag arrays [that] may be used to identify the function of identified open reading frames (ORFs) by creating deletion mutants for each ORF" and provisional patent application 60/140,359 as describing "methods of using tag arrays and the single base extension reaction for genotyping and other types of biological analysis." Page 10.

Discussion

1. Claims

Claims 1, 2, 7, and 15-19 are on appeal. Claim 1 is representative and reads as follows:

1. A set of nucleic acid tag probes comprising at least 1000 nucleic acid sequences chosen from the group consisting of:

SEQ ID NOS: 1-2000.

2. Utility

The examiner rejected claims 1, 2, 7, and 15-19 under 35 U.S.C. § 101 on the basis that the claimed nucleic acids lack patentable utility. The examiner reasoned that the

> specification does not teach the function of any of the nucleic acids to which these sequences hybridize. The function of these nucleic acids is as yet undetermined with no known biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the nucleic acid[s] of the instant application w[ere], as of the filing date, useful for any specific assay or therapeutic use.

Examiner's Answer, page 5. The examiner also found that the asserted utility as a tag was not specific: "Literally any sequence would function in a genome analysis assay as described in the specification" (id., page 5); "[t]hat is, when a nucleic acid is used solely as a tag, there is nothing specific to the particular sequence of the nucleic acid which renders it useful, but rather, it is the generic ability of all nucleic acids to hybridize to their complement which renders the nucleic acid useful" (id., page 16). The examiner concluded that the claimed nucleic acids lack the utility required by 35 U.S.C. § 101.

On its face, the examiner's position is not unreasonable – any nucleic acid will hybridize to its complement and therefore could be used, at least in theory, as a label.

In considering the utility of the instant claims, however, it is important to keep in mind that they are not directed to single nucleic acids chosen from the specification's SEQ ID NOs 1 to 2000. Rather, the claims are directed to a set of at least 1000 nucleic acids. Thus, the issue is not whether each nucleic acid individually has utility, but whether the specification adequately discloses a utility for a set of at least 1000 of the disclosed nucleic acids.

Appellants argue that the specification "assert[s] several specific and substantial utilities for the claimed invention." Appeal Brief, page 5. One method discussed in the Appeal Brief is "the use of tagged primers and an array of tag probes for genotyping polymorphisms." Page 7. "This method was described in greater detail in U.S. Patent Application No. 60/140,359, which is discussed in the present application at page 10, line 10 and was used in Fan et al. Genome Res. 10:853-860 (2000)." Appeal Brief, page 8. Appellants also argue that "the claimed sets of tags and tag probes were used to perform multiplex genotyping of 1,121 human single nucleotide polymorphisms from the SNP consortium (TSC) database. Hardenbol et al., Nat. Biotechnol., 21:673-8 (2003)." Appeal Brief, page 10.

Whether a claimed invention is supported by a patentable utility is determined based on what is disclosed in the patent application and what is known in the art as of the application's filing date. See In re Brana, 51 F.3d 1560, 1567 n.19, 34 USPQ2d 1436, 1441 n.19 (Fed. Cir. 1995) ("Enablement, or utility, is determined as of the application filing date.").

The instant application claims priority to provisional patent application 60/195,585, filed April 6, 2000. Specification, page 1. Fan appears to have been

published in June 2000 and Hardenbol was published in 2003. Appellants have not shown that the methods disclosed by Fan and Hardenbol were known to those of skill in the art as of the effective filing date of the present application. Thus, they cannot rely on the disclosures of those references to show that a patentable utility for the claimed nucleic acids would have been known to those of skill in the art.

The specification also cites patent application 08/626,285 and provisional patent application 60/140,359 as disclosing methods for using the claimed nucleic acids in tag arrays. See page 10, first and second full paragraphs. The specification also states that "[v]arious patents, patent applications and publications are referenced throughout the specification[;] unless otherwise indicated, each is incorporated by reference in its entirety for all purposes." Page 8, second paragraph.

Sources that are incorporated by reference into a patent application effectively become a part of the application. See Advanced Display Sys., Inc. v. Kent State Univ., 21 F.3d 1272, 1282, 54 USPQ2d 1673, 1679 (Fed. Cir. 2000) ("Incorporation by reference . . . makes clear that the material is effectively part of the host document as if it were explicitly contained therein.") (citations omitted). Thus, it might appear that the disclosures of the incorporated application and provisional application could be relied on, if they describe patentable utilities applicable to the claimed nucleic acids.

Essential material, however, can only be incorporated by reference to an issued U.S. patent or published U.S. patent application. See 37 CFR § 1.57(c):

> "Essential material" may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication. . . . "Essential material" is material that is necessary to (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

> terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . . .

Any disclosure that is required to meet the utility requirement of § 101 is necessarily required to meet the enablement requirement of § 112. See In re Ziegler, 992 F.2d 1197, 1200-01, 26 USPQ2d 1600, 1603 (Fed. Cir. 1993) ("The how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112." (citations omitted)).

If the methods described in the cited applications are necessary to support the utility of the present claims, then, they are "essential material," and to the extent that they would be relied on for describing a patentable utility for the claimed nucleic acids, they cannot properly be incorporated by reference into the specification.

Appellants also argue that

> [a] second utility asserted in the specification at page 10, lines 4-9, is the use of the tags for correlating specific mutations with phenotypic effects. . . . Deletion mutant strains that are each tagged with a different tag sequence are generated for each ORF, deleting a single ORF in each strain, and the resulting deletion mutants are grown under a wide variety of selective conditions. Detection of the tag sequence indicates survival of the deletion mutant under the selective conditions. This utility of the claimed invention is also described in U.S. Patent Application No. 08/626,285 (now U.S. Patent No. 6,458,530) which is incorporated by reference on page 10, line 5 of the specification, and is also described in Shoemaker et al. Nat. Genet. 14:450-456 (1996), a copy of which is provided herewith . . . and was previously provided for the Examiner's consideration with the amendment filed March 4, 2004.

Appeal Brief, page 9.

Appellants are correct that the specification states that application 08/626,285 was incorporated by reference. That incorporation, however, is ineffective to the extent that it is relied on to support the utility of the instant claims, for the reasons discussed above. In addition, U.S. Patent 6,458,530 cannot be relied on as evidence of the knowledge of those skilled in the art because it issued after the effective filing date of the instant application. See In re Glass, 492 F.2d 1228, 1231, 181 USPQ 31, 34 (CCPA 1974) ("[T]he contents of a patent application which may be available as 'prior art' under § 102(e) to show that another was the first inventor may not have been known to anyone other than the inventor, his attorney, and the Patent Office examiner . . . until it issued as a patent. As of its filing date it does not show what is known generally to 'any person skilled in the art,' to quote from § 112.").

Appellants also rely on the disclosure of Shoemaker[1] as evidence of the utility of the claimed nucleic acids. Shoemaker was published in 1996 and therefore is evidence of the knowledge of those skilled in the art as of this application's effective filing date (April 6, 2000).

Shoemaker describes a method of "molecular bar-coding" to identify strains of yeast deleted in different genes. Shoemaker states that "[e]ach deletion strain is labelled with a unique 20-base tag sequence that can be detected by hybridization to a high-density oligonucleotide array. The tags serve as unique identifiers (molecular bar codes) that allow analysis of large numbers of deletion strains simultaneously." Abstract.

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[1] Shoemaker et al., "Quantitative phenotypic analysis of yeast deletion mutants using a highly parallel molecular bar-coding strategy," Nature Genetics, Vol. 14, pp. 450-456 (1996).

> Shoemaker describes the tags as follows:
>
> The molecular tags are 20 base-pair DNA sequences specifically designed to serve as unique identifiers. Tag sequences are as different as possible yet still retain similar hybridization properties to facilitate simultaneous analysis on high-density oligonucleotide arrays. We used an algorithm to select a set of 9,105 maximally distinguished 20mer tag sequences that are predicted to have similar melting temperatures (61 ± 5 °C), no secondary structure and no extensive similarity between any two sequences in the list (>5 mismatches).

Page 451, last paragraph. Nucleic acids having sequences complementary to those of the molecular tags are synthesized on an array; particular deletion strains are identified based on hybridization between the tags and the nucleic acids on the array. See page 451, paragraph bridging the columns ("the molecular tags are . . . hybridized to a high-density array containing, at defined positions, known oligonucleotides that are complementary to the tag sequences").

We agree with Appellants that a person skilled in the art would have recognized the utility of the claimed nucleic acids in the method described by Shoemaker. While the instant specification does not describe the molecular bar-coding method in any detail, a specification need not teach what is known in the art. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1987) ("[A] patent need not teach, and preferably omits, what is well known in the art."

We also agree with Appellants that the molecular bar-coding method appears to be a specific and substantial utility for the claimed set of nucleic acids. The utility is specific because the Shoemaker states that nucleic acids used as tags should be maximally distinguished, yet have similar melting temperatures, no secondary structure, and no extensive similarity. Page 451.

The instant specification describes the nucleic acid sequences shown in SEQ ID NOs 1-2000 as having these properties. The specification states that the sequences were selected based on their hybridization characteristics: they have similar melting temperatures, were computationally filtered, do not match sequences in public databases, and show high discrimination and signal intensity when hybridized to their complements. Paragraph bridging pages 8 and 9. Thus, the nucleic acids of SEQ ID NOs 1-2000 appear to have hybridization properties suitable for use in the molecular bar-coding method described by Shoemaker.

In view of these specific, hybridization-related characteristics, we conclude that the examiner has not adequately supported his position that "any nucleic acid whatsoever has utility as a tag" (Examiner's Answer, page 13). Thus, the facts of this case distinguish the claimed set of nucleic acids from the ESTs at issue in In re Fisher, 421 F.3d 1365, 1374, 76 USPQ2d 1225, 1232 (Fed. Cir. 2005), in which the court concluded that the asserted utilities would apply to all ESTs. Here, the record supports Appellants' position (Reply Brief, page 4) that the utility of the claimed nucleic acids requires particular hybridization properties and therefore would not apply to all nucleic acids.

Using a set of nucleic acids in the molecular bar-coding method described by Shoemaker also appears to be a substantial utility. Shoemaker states that molecular bar-coding "allows large numbers of tagged deletion strains to be analysed simultaneously in a highly quantitative fashion" (page 453, last paragraph); that "molecular tags will also facilitate the task of keeping track of . . . thousands of deletion strains (page 454, last paragraph); and that "[t]he molecular bar-coding strategy . . . can

be applied to any task, in vitro or in vivo, that requires large populations (cells, DNA fragments, molecules, and so on) to be monitored in parallel" (page 455, first full paragraph). Thus, the record supports Appellants' position that the claimed set of nucleic acids has real-world utility as a research tool.

Again, the facts of this case distinguish it from In re Fisher. In that case, the court held that "the claimed ESTs act as no more than research intermediates that may help scientists isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes. . . . Accordingly, the claimed ESTs are, in the words of the Supreme Court, mere 'object[s] of use-testing,' to wit, objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end." 421 F.3d at 1373, 76 USPQ2d at 1231.

In this case, by contrast, the evidence shows that the claimed set of nucleic acids is useful in various research applications, including simultaneously assaying yeast deletion strains, and not merely as an object of further research that would provide no assurance of discovering anything that is actually useful.

The record supports Appellants' position that the specification discloses at least one specific and substantial utility for the claimed set of nucleic acids, which is all that 35 U.S.C. § 101 requires. See Juicy Whip Inc. v. Orange Bang Inc., 185 F.3d 1364, 1366, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999) ("An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit."). We therefore reverse the rejection based on 35 U.S.C. § 101.

3. Enablement

The examiner also rejected claims 1, 2, 7, and 15-19 under 35 U.S.C. § 112, first paragraph, as nonenabled. The reasoning underlying the rejection, however, is the same as that underlying the rejection under 35 U.S.C. § 101. The examiner has provided no basis on which to conclude that using the claimed nucleic acids in, for example, the method described by Shoemaker would have required undue experimentation. The rejection for lack of enablement is reversed for the reasons discussed above in regard to utility.

Summary

The record supports Appellants' position that the claimed set of nucleic acids has patentable utility based on their hybridization characteristics. Therefore, we reverse the rejections based on lack of utility.

REVERSED

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Administrative Patent Judge)
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